HPV-based primary screening for cervical cancer - status of implementation -

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I have no conflicts of interest to declare.
HPV
Viral characteristics

- non-enveloped viruses; icosahedral capsid

- remarkably diverse BUT remarkably genetically stable
  (diverged since the origin of humanity only by about 2%)

- classified by the homology of their genome into many genotypes

- genotypes numbered chronologically in order of characterization
  (222 official HPV genotypes, HPV-226 last officially appointed genotype)
Cancers attributable to HPV:
- 4.5% of all cancers worldwide
- 630,000 new cancer cases per year
- 8.6% of all cancers in women
- 0.8% of all cancers in men

GLOBOCAN 2012 data
High-risk alpha HPV genotypes

HPV-16, HPV-18, HPV-31, HPV-33, HPV-35, HPV-39
HPV-45, HPV-51, HPV-52, HPV-56, HPV-58, HPV-59
HPV DNA is found in virtually all cases of cervical cancer.

HPV is a necessary cause of cervical cancer.

The association between persistent HPV infection and cervical carcinoma is very strong, consistent, specific, and universal (>15 times stronger than that between cigarette smoking and lung cancer).

Cervical cancer only exceptionally develops in the absence of the persistent presence of HPV DNA.
WHO leads the way towards the elimination of cervical cancer as a public health concern

September 2018 | Cervical cancer is a grave threat to women's health and lives, and globally, one woman dies of cervical cancer every two minutes. This suffering is unacceptable, particularly as cervical cancer is largely preventable.

Cervical cancer screening and prevention, Zambia
secondary prevention (screening)
(cytology, HPV, cytology + HPV)
+
primary prevention (vaccination)
secondary and primary prevention act additively by intervening at different points in the natural history of cervical cancer and imply actions in women of different ages
Impact of scaled up human papillomavirus vaccination and cervical screening and the potential for global elimination of cervical cancer in 181 countries, 2020–99: a modelling study

Kate T Simms, Julia Steinberg, Michael Caruana, Megan A Smith, Jie-Bin Lew, Isabelle Soerjomataram, Philip E Castle, Freddie Bray, Karen Canfell

Lancet Oncol 2019;20:394-407
secondary prevention (screening)
(cytology-based, **HPV-based**, cytology + HPV-based)
Cervical cancer is an appropriate disease for screening

- important public health issue (569'847 cases per year; 311'365 deaths in 2018)
- precursors lesions can be treated in a safe, effective and acceptable way
- long clinical latency
- acceptable and valid screening tools

The major goal of cervical screening programs is to find pre-cancers that can be treated to prevent invasive cancers
population-based & organised & high coverage & high quality cytology
Status of implementation and organization of cancer screening in The European Union Member States—Summary results from the second European screening report

Partha Basu, Antonio Ponti, Ahti Anttila, Guglielmo Ronco, Carlo Senore, Diama Bhadra Vale, Nereo Segnan, Mariano Tomatis, Isabelle Soerjomataram, Maja Primic Žakelj, Joakim Dillner, Klara Miriam Elfström, Stefan Lönnberg and Rengaswamy Sankaranarayanan

Int J Cancer 2018; 142: 44-56

<table>
<thead>
<tr>
<th>Cervical cancer screening (target age 30–59 years)</th>
<th>Population-based programme</th>
<th>Non-population based programme or no programme</th>
<th>TOTAL</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rollout completed</td>
<td>Rollout ongoing</td>
<td>Piloting</td>
</tr>
<tr>
<td>Number of Member States in 2016</td>
<td>9</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Number of Member States in 2007</td>
<td>7</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Estimated target populations in 2016</td>
<td>34.7 M (32.5%)</td>
<td>24.1 M (22.7%)</td>
<td>0.02 M (0.0%)</td>
</tr>
<tr>
<td>Estimated target populations in 2007</td>
<td>24.1 M (22.7%)</td>
<td>21.9 M (20.6%)</td>
<td>5.3 M (5.0%)</td>
</tr>
</tbody>
</table>
The type and implementation status of the cervical cancer screening programmes in the Member States of European Union (2016)
## Incidence of cervical cancer in Slovenia 2003-2016

<table>
<thead>
<tr>
<th>year</th>
<th>annual number of new cases</th>
<th>crude incidence rate/100,000</th>
<th>ASR (W)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>211</td>
<td>20.7</td>
<td>15.3</td>
</tr>
<tr>
<td>2004</td>
<td>198</td>
<td>19.4</td>
<td>13.7</td>
</tr>
<tr>
<td>2005</td>
<td>182</td>
<td>17.8</td>
<td>12.7</td>
</tr>
<tr>
<td>2006</td>
<td>162</td>
<td>15.8</td>
<td>11.3</td>
</tr>
<tr>
<td>2007</td>
<td>154</td>
<td>15.0</td>
<td>10.5</td>
</tr>
<tr>
<td>2008</td>
<td>130</td>
<td>12.6</td>
<td>8.8</td>
</tr>
<tr>
<td>2009</td>
<td>131</td>
<td>12.6</td>
<td>8.8</td>
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<tr>
<td>2010</td>
<td>142</td>
<td>13.7</td>
<td>9.4</td>
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<td>2011</td>
<td>142</td>
<td>13.7</td>
<td>9.0</td>
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<td>2012</td>
<td>118</td>
<td>11.4</td>
<td>7.7</td>
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<tr>
<td>2013</td>
<td>124</td>
<td>11.9</td>
<td>8.0</td>
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<td>2014</td>
<td>114</td>
<td>11.0</td>
<td>6.8</td>
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<tr>
<td>2015</td>
<td>119</td>
<td>11.4</td>
<td>7.4</td>
</tr>
<tr>
<td>2016</td>
<td>123</td>
<td>11.8</td>
<td>7.8</td>
</tr>
</tbody>
</table>

**opportunistic screening**
- coverage app. 40%
- 169,231 smears/year

**organised screening**
- coverage above 70%
- 170,861 smears/year

**ASR (W):** age-standardized rate by world population
Cervical Cancer Incidence: Europe

Cervical cancer: Age-standardised incidence rate per 100,000 women

Source: Globocan 2018
cytology-based screening

HPV-based screening
Global evaluation of the sensitivity (fraction of histology confirmed CIN 2+ detected by the test) of HPV tests as compared to cytology in studies in Europe and North America

- HART
- Tuebingen
- Hannover
- Jena
- French Public
- French Private
- Seattle
- Canada
- Italy

Combined

Positivity

- Point estimates and 95% C.I. The size of the box is proportional to the size of the study.
- Summary estimates of all studies.
HPV-based screening provides 60-70% greater protection against invasive cervical carcinomas compared with cytology.
Cumulative risk of CIN+2, CIN3+ and cervical cancer among 1,011,092 women aged 30 to 64 years at Kaiser Permanente Northern California by enrollment Pap and HPV test result; 2003 to 2012.

HPV Screening for Cervical Cancer in Rural India

HPV-based primary cervical cancer screening

**PRO:**
- more sensitive than cytology to detect CIN2+, CIN3+ and cervical cancer
- more accurate and less variable than cytology
- risk of CIN2+ in women who are HPV negative is substantially lower than in women who are cytologically negative = extension of screening intervals possible and safe
- possibility of self-sampling testing

**CON:**
- reduced specificity of HPV DNA testing requires appropriate triage
Cervical cancer screening

HPV-testing and cytology (co-testing)

HPV-testing or cytology

Triage of HPV screen-positives

partial genotyping (HPV-16 and HPV-18)

cytology
Relative sensitivity of HPV primary testing in combination with cytology versus HPV primary testing alone

2015 European guidelines for quality assurance in cervical cancer screening
USPSTF recommends screening for cervical cancer:

every 3 years with cervical cytology alone in women aged 21 to 29 years (A recommendation)

screening every 3 years with cervical cytology alone, every 5 years with hrHPV testing alone, or every 5 years with hrHPV testing in combination with cytology (co-testing) in women aged 30 to 65 years (A recommendation)

against screening for cervical cancer in women younger than 21 years (D recommendation)
HPV !!!
HPV test ?
European guidelines for quality assurance in cervical cancer screening. Summary of the supplements on HPV screening and vaccination

Lawrence von Karsa a,*, Marc Arbyn b, Hugo De Vuyst c, Joakim Dillner d, Lena Dillner e, Silvia Franceschi f, Julietta Patnick g, Guglielmo Ronco h, Nereo Segnan h, Eero Suonio a, Sven Törnberg i, Ahti Anttila j

**HPV test choice**

cervical cancer screening program should adopt a HPV primary test for use only if it has been validated by demonstrating reproducible, consistently high sensitivity for CIN2+ and CIN3+ lesions, and only minimal detection of clinically irrelevant, transient HPV infection

HPV tests (neither commercial nor in-house tests) that have not been clinically validated should not be used in clinical practice
BUFFALO BILL'S WILD WEST
AND CONGRESS OF ROUGH RIDERS OF THE WORLD.

A COMPANY OF WILD WEST COWBOYS.
THE REAL ROUGH RIDERS OF THE WORLD WHOSE DARING EXPLOITS
HAVE MADE THEIR VERY NAMES SYNONYMOUS WITH DEEDS OF BRAVERY.

COL. W. F. CODY
BUFFALO BILL
WILL APPEAR
AT EVERY PERFORMANCE.
2010  70 commercial HPV assays on the market

2012  125 commercial HPV assays (and 84 variants) on the market

2015  193 commercial HPV assays (and 127 variants) on the market

2017  246 commercial HPV assays (and 214 variants) on the market

- only 30.1% of HPV tests with published evaluation (analytical and/or clinical)
- “test A versus test B” approach with no reference standard
- ad hoc collections of heterogeneous clinical samples without follow-up
Which high-risk HPV assays fulfil the criteria for use in primary cervical cancer screening?
Which high-risk HPV assays fulfil the criteria for use in primary cervical cancer screening?

**Regulatory approvals**

US Food and Drug Administration (FDA) approval

**Co-testing (every 5 years, >=30 years)**

- Hybrid Capture 2 (hc2) HPV DNA Test (Qiagen)
- Cervista HPV HR Test + Cervista HPV 16/18 Test (Hologic)
- APTIMA HPV Assay + APTIMA HPV 16 18/45 genotype assay (Hologic)
- cobas 4800 HPV Test (Roche)
- BD Onclarity HPV assay (BD)

**HPV testing only (every 3 years, >=30 years)**

- cobas 4800 HPV Test (Roche)
- BD Onclarity HPV assay (BD)
Which high-risk HPV assays fulfil the criteria for use in primary cervical cancer screening?

Regulatory approvals

US Food and Drug Administration (FDA) approval

Academic validations

- International guidelines (Meijer's criteria)
- Valgent 1-4
- Academic multi-test comparisons (PREDICTORS 3)
Which high-risk HPV assays fulfil the criteria for use in primary cervical cancer screening?

**Regulatory approvals**

US Food and Drug Administration (FDA) approval

**Academic validations**

- International guidelines (Meijer's criteria)
- Valgent 1-4
- Academic multi-test comparisons (PREDICTORS 3)
relative clinical accuracy compared to either of two HPV tests which demonstrated lower cumulative incidence of cervical cancer 5 years after a negative HPV test than 3 years after a normal cytology in four large European randomized trials
Requirements for HPV tests in primary cervical screening

1. A clinical sensitivity for CIN2+ not less than 90% of the clinical sensitivity of the hc2 in women of at least 30 years.

2. A clinical specificity for CIN2+ not less than 98% of the clinical specificity of the hc2 in women of at least 30 years of age.

3. Intra-laboratory reproducibility and inter-laboratory agreement with a lower confidence bound not less than 87%.
Which high-risk HPV assays fulfil the criteria for use in primary cervical cancer screening?

Regulatory approvals

US Food and Drug Administration (FDA) approval

Academic validations

- International guidelines (Meijer's criteria)
- Valgent 1-4
- Academic multi-test comparisons (PREDICTORS 3)
VALGENT 1
5 HPV assays - samples derived from a Belgian biobank

VALGENT 2
6 HPV assays - samples derived from Scottish HPV archive

VALGENT 3
13 HPV assays - samples derived from Slovenian national cohort

VALGENT 4
11 HPV assays - samples from Copenhagen, Denmark
Which high-risk HPV assays fulfil criteria for use in primary cervical cancer screening?

M. Arbyn¹, P. J. F. Snijders², C. J. L. M. Meijer², J. Berkhof³, K. Cuschieri⁴, B. J. Kocjan⁵ and M. Poljak⁵

1) Unit of Cancer Epidemiology and Belgian Cancer Centre, Scientific Institute of Public Health, Brussels, Belgium, 2) Department of Pathology, 3) Department of Clinical Epidemiology and Biostatistics, VU University Medical Centre, Amsterdam, The Netherlands, 4) Scottish HPV Reference Laboratory, Royal Infirmary of Edinburgh, Edinburgh, Scotland, UK and 5) Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

UPDATE OF THE LIST OF HPV ASSAYS THAT FULFILL REQUIREMENTS FOR PRIMARY CERVICAL CANCER SCREENING


submitted
Hybrid Capture 2 (hc2) HPV DNA Test (Qiagen)  
EIA kit HPV GP HR (Labo Bio-medical Products)  
cobas 4800 HPV Test (Roche)  
APTIMA HPV Assay (Hologic)  
Cervista HPV HR Test (Hologic)  
RealTime High Risk HPV test (Abbott)  
PapilloCheck HPV-screening test (Greiner Bio-One)  
Real-time quantitative PCR (qPCR) assay targeting the E6 and E7 genes (Riatol - Belgian private lab)  
HPV-Risk assay (Self-Screen)  
BD Onclarity HPV Assay (Becton Dickinson)  
LMNX genotyping kit HPV GP HR (Labo Bio-medical Products) - previous digene HPV Genotyping LQ Test  
Anyplex II HPV HR (Seegene)  
Xpert HPV (Cepheid)  
EUROArray HPV Test (EuroImmun)  
Linear Array HPV Genotyping Test (Roche) - restricted to 13 hrHPV types
HPV tests with at least 36+ months longitudinal data

Hybrid Capture 2 (hc2) HPV DNA Test (Qiagen)
EIA kit HPV GP GP5+/6+ HR
cobas 4800 HPV Test (Roche)
RealTime High Risk HPV test (Abbott)
APTIMA HPV Assay (Hologic, Gen-Probe)
- 246+ commercial HPV assays (and 214+ variants) on the market
- 2 + 11 HPV assays fulfil cross-sectional criteria for primary screening
- 2 + 3 HPV assays have at least 36+ months longitudinal data
European guidelines for quality assurance in cervical cancer screening
Second edition - Supplements
HPV laboratory choice

HPV testing should be performed only on samples processed and analyzed in qualified laboratories, accredited by authorized accreditation bodies and in compliance with international standards.

The laboratory should perform a minimum of 10,000 HPV tests per year.
General recommendations

primary HPV testing can be used only in a population-based program for cervical cancer screening

HPV testing outside population-based programs is not recommended
Screening age

routine HPV primary screening can begin at age of 35 years or above and should not begin under age of 30 years
Prevalence of infection with 14 hr-HPV types with 95% confidence intervals according to age among 4,431 women screened for cervical cancer, Slovenia, 2010.
model of cervical cancer natural history calibrated to data to simulate the remaining lifetime risk of cervical cancer
cervical cancers could be prevented in later life with cytology screening up to age 75 years
negligible benefit in screening women with a negative HPV test after age 55 years
Screening interval

the screening interval for women with a negative HPV primary test result should be at least 5 years and may be extended up to 10 years depending on the age and screening history
Safety of extending screening intervals beyond five years in cervical screening programmes with testing for high risk human papillomavirus: 14 year follow-up of population based randomised cohort in the Netherlands

Maaike G Dijkstra,1,2 Marjolein van Zummeren,1 Lawrence Rozendaal,1 Folkert J van Kemenade,3 Theo J M Helmerhorst,4 Peter J F Snijders,1 Chris J L M Meijer,1 Johannes Berkhof5

Cumulative incidence of cervical cancer and CIN3+ per trial group and baseline screening result, after up to three screening rounds
**Secondary testing - Cytology triage**

women testing positive for oncogenic HPV at primary screening should be tested without delay for cervical cytology (cytology triage)

direct referral to colposcopy of all HPV-positive women is not recommended

the cytology test should preferably use the specimen collected during the HPV screening visit

women who have negative cytology at triage after a positive initial HPV primary test in a screening episode should be followed up by re-testing after an interval shorter than the regular screening interval, but after at least 6-12 months
<table>
<thead>
<tr>
<th>Baseline triage test</th>
<th>Repeat test at 12 months</th>
<th>hr-HPV-positive women</th>
<th>Total screening population</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Endpoint CIN3+</td>
<td>Colposcopy</td>
</tr>
<tr>
<td></td>
<td></td>
<td>NPV% (95%CI)</td>
<td>Referral rate% (95%CI)</td>
</tr>
<tr>
<td>Cytology</td>
<td>Cytology</td>
<td>99.3 (98.1-99.8)</td>
<td>1.70 (1.54-1.85)</td>
</tr>
<tr>
<td>Cytology</td>
<td>HPV type persistence</td>
<td>97.5 (95.2-98.7)</td>
<td>2.45 (2.26-2.64)</td>
</tr>
<tr>
<td>Cytology</td>
<td>Cytology &amp; HPV16/18</td>
<td>99.5 (98.1-99.9)</td>
<td>2.31 (2.12-2.49)</td>
</tr>
<tr>
<td>Cytology &amp; HPV-16/18</td>
<td>Cytology</td>
<td>99.7 (98.4-99.9)</td>
<td>2.53 (2.34-2.73)</td>
</tr>
</tbody>
</table>

CI = confidence interval; NPV = negative predictive value

Table 2.

NPV and colposcopy referral rates for four triage strategies for hr-HPV-positive women based on baseline and one round of repeat testing, adjusted for non-attendance at repeat testing.

Applicable only in countries where the quality of cytology is high and the screening interval is long (5 years).
Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses

Marc Arbyn,¹ Sara B Smith,² Sarah Temin,³ Farhana Sultana,⁴,⁵ Philip Castle,²,⁶ on behalf of the Collaboration on Self-Sampling and HPV Testing
HPV-based cervical screening in Europe

The Netherlands

- national organized program started in Jan 2017; only HPV testing
- all women aged 30, 35, 40, 50 and 60
- women aged 45 and 55: if they did not participate five years previously or if they were hrHPV-positive five years ago
- women aged 65: if they were hrHPV-positive five years ago
- clinical samples (GPs, ThinPrep) and self sampling (Evalyn Brush) for non-responders
- triage of HPV positives by cytology (baseline and 6-12 months later)
- only 5 accredited labs (down to 40 cytology labs); 450 samples daily/lab
- central tender for: labs, HPV test (Roche Cobas 4800), self-sampling device
HPV-based cervical screening in Europe
The Netherlands

Clinician collected samples: 9% hrHPV positive
Self-collected samples: 7% hrHPV positive
HPV-based cervical screening in Europe
The Netherlands
HPV-based cervical screening in Europe

The Netherlands

www.rivm.nl
HPV-based cervical screening in Europe

Turkey

- HPV-based national organized program started in 2013
- HPV primary testing (hc2); reflex triage HPV16/18 + cytology
- women aged 30-65 years old; 5-years interval
- samples taken by GPs and trained nurses
- two HPV laboratories in Ankara and Istanbul (1 million HPV tests per year)

- over 4 million tests performed 2013-2018; hrHPV positivity = 4.43% !!!
- screening rate in organised (cytology-based) program in 2012 = 2%
- screening rate in organised (HPV-based) program in 2018 = 36.5%

Initial results of population based cervical cancer screening program using HPV testing in one million Turkish women

Murat Gultekin, Müjdegül Zayifoglu Karaca, Irem Kucukyildiz, Selin Dundar, Güledal Boztas, Hatice Semra Turan, Ezgi Hacikamiloğlu, Kamil Murtuza, Bekir Keskinkılıç and Irfan Sencan

HPV-based cervical screening in Europe

Mega HPV laboratories for cervical cancer control: Challenges and recommendations from a case study of Turkey

Murat Gultekin, Mujde Zayifoglu Karaca, Irem Kucukyildiz, Selin Dundar, Bekir Keskinkilic, Murat Turkyilmaz

Papillomavirus Research 7 (2019) 118–122
HPV-based cervical screening in Europe

Italy

- 5 regions started HPV-based screening in 2015/2016; national program soon?
- women 30-64 years; 5-year interval; triage by cytology or HPV16/18 genotyping
- different (but all clinically validated) HPV tests in use

![Proportion of women invited for HPV](image)

<table>
<thead>
<tr>
<th>Region</th>
<th>Proportion</th>
</tr>
</thead>
<tbody>
<tr>
<td>CALABRIA</td>
<td>0.7%</td>
</tr>
<tr>
<td>LOMBARDIA</td>
<td>2.1%</td>
</tr>
<tr>
<td>VALLE D’AOSTA</td>
<td>4.4%</td>
</tr>
<tr>
<td>LIGURIA</td>
<td>4.9%</td>
</tr>
<tr>
<td>CAMPANIA</td>
<td>8.7%</td>
</tr>
<tr>
<td>TRENTO</td>
<td>11.9%</td>
</tr>
<tr>
<td>LAZIO</td>
<td>22.1%</td>
</tr>
<tr>
<td>TOSCANA</td>
<td>27.2%</td>
</tr>
<tr>
<td>EMILIA ROMAGNA</td>
<td>33.5%</td>
</tr>
<tr>
<td>PIEMONTE</td>
<td>43.9%</td>
</tr>
<tr>
<td>BASILICATA</td>
<td>44.8%</td>
</tr>
<tr>
<td>VENETO</td>
<td>64.6%</td>
</tr>
<tr>
<td>MOLISE</td>
<td>82.8%</td>
</tr>
<tr>
<td>UMBRIA</td>
<td>84.3%</td>
</tr>
<tr>
<td>ABRUZZO</td>
<td>89.0%</td>
</tr>
<tr>
<td>ITALY</td>
<td>22.9%</td>
</tr>
</tbody>
</table>

Target age:
- 25-64
- 30-64
- 45-64
- 70-64

Courtesy by Paolo Giorgi Rossi
HPV-based cervical screening in Europe

Near future.....

Sweden
- since 2015 HPV screening recommended for women ages 30-64 after successful randomized health services study performed between 2012-2016 which enrolled 400,000 women;
- 9/21 regions in Sweden implemented or partially implemented HPV screening as of March 2019

Norway
- randomized implementation 2015-2017; gradual national implementation during 2019-2021;
- 25-33 years: cytology in 3-year interval; 34-69 years: HPV testing in 5-years intervals

Denmark
- implementation by January 2020, 2nd triage method under consideration (CINTEC+ and/or partial genotyping)
HPV-based cervical screening in Europe
Near future.....

UK
- 25-65 years; 3 yearly recall until aged 50, then every 5 years; Wales initiated program in 2018, England & Scotland & North Ireland due to initiate in 2019/2020

Belgium
- cytology 25-29 years; HPV-based screening age 30-64 at 5 years interval; triage reflex cytology; decided in July 2018 - preparation period 2 years

Germany
- implementation by 2020 (?); 20-30 years: annual cytology; 30-34: annual cytology + HPV co-testing; above 35 years: cytology + HPV co-testing every three years
Australia has a comprehensive organised screening program since 1991, which by 2010 had already halved cervical cancer incidence rates.

- prompted by the exceptional impact of HPV vaccination transition from 2-year cytology screening to 5-yearly HPV-based screening in December 2017.
- HPV test with partial HPV genotyping and reflex liquid based cytology triage, for HPV vaccinated and unvaccinated women 25–69 years of age, with exit testing of women up to 74 years of age.
- self collection for an under-screened or never-screened woman facilitated by a medical or nurse practitioner.
- transition expected to reduce cervical cancer incidence and mortality rates by at least a further 20%.
vaccination of women with the 9v vaccine from 2018 onwards and discontinuation of cervical screening in women offered this vaccination

continuing vaccination with the 9v vaccine and continuation of screening as per the existing National Cervical Screening Program
HPV-based cervical screening

United States

- the first country to approve and recommend HPV tests for screening
- there is no organized screening program in the US
- in most settings screening recommendations are not binding and are not enforced except in some cases via insurance reimbursement policies
- three options available: cytology, HPV testing, co-testing, which differ by starting age, screening interval and management
- abundance of choices is challenging for providers and has led to a lot of confusion
- poor implementation with a strong tendency to screen much more frequently than needed
- cervical cancer screening is currently undergoing a major transition
We know HPV is causing cervical cancer

We have excellent HPV screening tests and HPV vaccines

We can envisage cervical cancer elimination